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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/438,365	11/12/1999	Yongliang Chu	0942.4650001	9217

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EXAMINER

EPPS, JANET L

ART UNIT	PAPER NUMBER
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1635

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DATE MAILED: 07/03/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/438,365

Applicant(s)

CHU ET AL.

Examiner

Janet Epps

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 18 April 2002.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-112 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-9, 11, 15, 20, 21, 29, 42, 45, 48, 63, 70, 77 and 93-110 is/are rejected.
- 7) ☒ Claim(s) 10, 12-14, 16-19, 22-28, 43-44, 46-47, 49-62, 64-69, 71-76, 78-92 and 111-112 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other:

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DETAILED ACTION

Response to Arguments

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

2. Claims 1-9, 11, 15, 20-21, 29, 42, 45, 48, 63, 70, 77, 93, and 95-110 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for synthesizing and using compounds according to the present invention wherein the Q+ moiety is N (nitrogen), does not reasonably provide enablement for synthesizing and using compounds wherein the Q+ moiety is S (sulfur) or O (oxygen). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims, for the reasons of record set forth in the Official Action mailed 12-17-01.

Applicant's arguments filed 5-09-2002 have been fully considered but they are not persuasive. Applicants traverse the instant rejection on the grounds that Applicant is not limited to the confines of the specification to provide the necessary information to enable the invention, since they are not obligated to supply information that is well known in the art or that which is common and well known. Secondly, Applicant may incorporate by reference the necessary information by citing to certain types of documents that contain this information. Moreover, Applicants argue that the specification need not contain a single working example. Finally Applicants argue that the examiner has not considered the various factors articulated in *In re Wands*.

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In the instant case Applicants claim an exponential number of compounds, wherein said compounds comprise a variety of Markush substitutions and further wherein said compounds comprise chemically distinct central groups, namely O, S, and N. In particular, the instantly claimed compounds encompass compounds wherein the Q^+ moiety is quaternally substituted and positively charged, neither the specification as filed nor the prior art provides sufficient guidance to make and/or use compounds according to the present invention comprising either O^{+4} or S^{+4} moieties. Although Applicants argue that N, S, and O are bioisosters, and thus, exhibit similar chemical and physical properties, and produce similar biological properties. However, contrary to Applicant's assertions, Thornber (1979) clearly states that in regards, to size, shape, electronic distribution, lipid and water solubility, pKa, chemical reactivity, and hydrogen bonding capacity, it is unlikely that any bioisosteric replacement will leave all these parameters undisturbed. (*emphasis added*). It is unclear, according to Thornber, what parameter will be affected with a bioisosteric replacement, therefore even with bioisosteric substitutions there is a degree of unpredictability. Moreover, in regards to Applicants citing documents such as Haces et al. to support the enablement of the instant invention, it is noted that unless the Haces et al. reference discloses the compounds of the present invention, it is unclear how the teachings of Haces et al. are to be modified in order to provide a method that produce the compounds according to the present invention. It is noted that Haces et al. does not disclose compounds wherein either O or S are quaternally substituted and positively charged. Although Applicants argue that in regards to the degree of substitution in compounds of formula (A) where Q^+ is S or O, it would be obvious for a skilled person that when Q is O or S, the number of substituents should be according to their valency, however, it is noted that the features upon which applicant relies are

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not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). It is further noted that Applicants do not refer to a portion of the specification describing the charged Q⁺ moiety as recited in claim 93.

In regards to Applicant's assertions that the examiner has not considered the *Wands* factors in the formulation of the rejection of lack of enablement. It is noted that while the analysis and conclusion of a lack of enablement are based on the *Wands* factors as discussed in MPEP § 2164.01(a) and the evidence as a whole, it is not necessary to discuss each factor in the written enablement rejection. Contrary to Applicant's assertions, the language of the prior Office Action focused on those factors, and provided reasons that lead the examiner to conclude that the specification fails to teach how to make and use the claimed invention without undue experimentation, or that the scope of any enablement provided to one skilled in the art is not commensurate with the scope of protection sought by the claims.

As stated in the prior Office Action, Applicants have not provided one example wherein a compound according to general formula (A) is substituted with either O or S in the Q⁺ position. Furthermore, Applicants have only demonstrated the delivery of plasmid DNA into human embryonic kidney cells comprising the use of compounds wherein the Q⁺ moiety is N as described above. There are no examples wherein Applicants have either synthesized compounds wherein Q⁺ is either S or O, and further wherein Applicants have used these compounds for the delivery of macromolecules into cells. Moreover, due to the differences in the chemical properties between Oxygen, Sulfur, and Nitrogen, one of skill in the art would not accept on its

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face that the synthetic route for the compounds according to the present invention wherein Q+ is N is readily amenable for the synthesis of compounds wherein the Q+ moiety is either O or S. Based upon the lack of disclosure with regards to the synthetic steps required to synthesize the full breadth of compounds encompassed by the Markush structure recited in claims 1, 93, and 110, and the lack of working examples wherein Applicants have successfully synthesized compounds wherein Q+ is either S or O, and wherein Applicants have used said compounds for delivery of macromolecules in the cells, one of ordinary skill in the art would have to resort to trial and error experimentation in order to practice the full scope of the claimed invention.

The quantity of experimentation required to practice the invention as claimed would require determining the synthetic routes for isolating the full scope of the compounds encompassed by the instant claims, and further determining if said compounds are suitable as transfection agents. The specification as filed provides only guidelines with regards to substituted amine compounds according general formula (A). The deficiencies in the specification would constitute undue experimentation since the steps required for the chemical preparation of compounds according to general formula (A) wherein Q+ is either S or O, must be determined without instructions from the specification before one is enabled to practice the claimed invention.

Conclusion

3. Claims 10, 12-14, 16-19, 22-28, 43-44, 46-47, 49-62, 64-69, 71-76, 78-92, and 111-112 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

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4. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

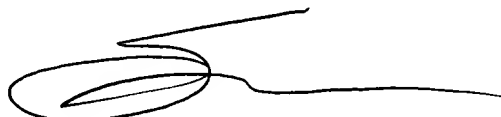
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5. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Epps whose telephone number is 703-308-8883. The examiner can normally be reached on Mondays through Friday, 9:00AM to 6:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader can be reached on (703)-308-0447. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-305-7939 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

jle
June 24, 2002



SEAN McGARRY
PRIMARY EXAMINER
1635